

IN THE CLAIMS

Claim 1(original): An isolated nucleic acid encoding a protein molecule shown in SEQ ID NO. 1.

Claim 2(original): An isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is a DNA molecule.

Claim 3(original): An isolated nucleic acid molecule of claim 2, wherein the nucleic acid molecule is a cDNA molecule, in particular a cD N A molecule comprising a nucleotide sequence shown in SEQ ID NO. 2 or SEQ ID NO. 3.

Claim 4(original): An isolated D N A molecule capable of hybridizing with the complement of the cD N A described in SEQ ID NO. 2 or SEQ ID NO. 3 under stringent condition.

Claim 5(currently amended): A vector comprising a nucleic acid molecule according to claim 1 ~~one of claims 1 to 4~~.

Claim 6(original): A vector according to claim 5 wherein said vector is a plasmid, a virus or a bacteriophage.

Claim 7(currently amended): A cell transformed with a nucleic acid molecule according to claim 1 ~~one of claims 1 to 4~~, wherein said cell is in particular a bacterial cell, a yeast cell, a mammalian cell, or an insect cell.

Claim 8(original): A protein molecule shown in SEQ ID NO. 1.

Claim 9(original): A protein molecule shown in SEQ ID NO. 1, or a fragment, or derivative, or variant thereof, for use as a diagnostic target for detecting a neurodegenerative disease, preferably Alzheimer's disease.

Claim 10(original): A protein molecule shown in SEQ ID NO. 1, or a fragment, or derivative, or variant thereof, for use as a screening target for reagents or compounds preventing, or treating, or ameliorating a neurodegenerative disease, preferably Alzheimer's disease.

Claim 11(original): An antibody specifically immunoreactive with an immunogen, wherein said immunogen is a protein molecule shown in SEQ ID NO. 1, or a fragment, or derivative, or variant thereof.

Claim 12(original): Use of an antibody of claim 11, for detecting the pathological state of a cell in a sample from a subject, comprising immunocytochemical staining of said cell with said antibody, wherein an altered degree of staining, or an altered staining pattern in said cell compared to a cell representing a known health status indicates a pathological state of said cell.

Claim 13(original): A method of diagnosing or prognosticating a neurodegenerative disease in a subject, or determining whether a subject is at increased risk of developing said disease, comprising: determining a level and/or an activity of

- (i) a transcription product of the gene coding for hTARPP, and/or
- (ii) a translation product of the gene coding for hTARPP, and/or

(iii) a fragment, or derivative, or variant of said transcription or translation product, in a sample from said subject and comparing said level and/or said activity to a reference value representing a known disease or health status, thereby diagnosing or prognosticating said neurodegenerative disease in said subject, or determining whether said subject is at increased risk of developing said neurodegenerative disease.

Claim 14(original): A method of monitoring the progression of a neurodegenerative disease in a subject, comprising: determining a level and/or an activity of

- (i) a transcription product of the gene coding for hTARPP, and/or
- (ii) a translation product of the gene coding for hTARPP, and/or
- (iii) a fragment, or derivative, or variant of said transcription or translation product, in a sample from said subject and comparing said level and/or said activity to a reference value representing a known disease or health status, thereby monitoring the progression of said neurodegenerative disease in said subject.

Claim 15(original): A method of evaluating a treatment for a neurodegenerative disease, comprising:

determining a level and/or an activity of

- (i) a transcription product of the gene coding for hTARPP, and/or
- (ii) a translation product of the gene coding for hTARPP, and/or

- (iii) a fragment, or derivative, or variant of said transcription or translation product, in a sample from a subject being treated for said disease and comparing said level and/or said activity to a reference value representing a known disease or health status, thereby evaluating said treatment for said neurodegenerative disease.

Claim 16(currently amended): The method according to claim 13 ~~any of claims 13 to 15~~ wherein said neurodegenerative disease is Alzheimer's disease.

Claim 17(currently amended): The method according to claim 13 ~~any of claims 13 to 16~~ wherein said sample comprises a cell, or a tissue, or a body fluid, in particular cerebrospinal fluid or blood.

Claim 18(currently amended): The method according to claim 13 ~~any of claims 13 to 17~~ wherein said reference value is that of a level and/or an activity of

- (i) a transcription product of the gene coding for hTARPP, and/or
- (ii) a translation product of the gene coding for hTARPP, and/or
- (iii) a fragment, or derivative, or variant of said transcription or translation product, in a sample from a subject not suffering from said neurodegenerative disease.

Claim 19(currently amended): The method according to claim 13 ~~any of claims 13 to 18~~ wherein an alteration in the level and/or activity of a transcription product of the gene coding for hTARPP and/or a translation product of the gene

coding for hTARPP and/or a fragment, or derivative, or variant thereof, in a sample cell, or tissue, or body fluid, in particular cerebrospinal fluid, from said subject relative to a reference value representing a known health status indicates a diagnosis, or prognosis, or increased risk of Alzheimer's disease in said subject.

Claim 20(original): A kit for diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, in a subject, or determining the propensity or predisposition of a subject to develop such a disease, said kit comprising:

- (a) at least one reagent which is selected from the group consisting of
 - (i) reagents that selectively detect a transcription product of the gene coding for hTARPP, and (ii) reagents that selectively detect a translation product of the gene coding for hTARPP, and
- (b) an instruction for diagnosing, or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, or determining the propensity or predisposition of a subject to develop such a disease by
 - detecting a level, or an activity, or both said level and said activity, of said transcription product and/or said translation product of the gene coding for hTARPP, in a sample from said subject; and
 - diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, or determining the propensity or predisposition of said subject to develop such a disease,wherein a varied level, or activity, or both said level and said activity, of said transcription product and/or said translation product compared to a reference

value representing a known health status, or wherein a level, or activity, or both said level and said activity, of said transcription product and/or said translation product similar or equal to a reference value representing a known disease status indicates a diagnosis or prognosis of a neurodegenerative disease, in particular Alzheimer's disease, or an increased propensity or predisposition of developing such a disease.

Claim 21(original): A method of treating or preventing a neurodegenerative disease, in particular Alzheimer's disease, in a subject comprising administering to said subject in a therapeutically or prophylactically effective amount an agent or agents which directly or indirectly affect an activity and/or a level of (i) a gene coding for hTARPP, and/or (ii) a transcription product of the gene coding for hTARPP, and/or (iii) a translation product of the gene coding for hTARPP, and/or (iv) a fragment, or derivative, or variant of (i) to (iii).

Claim 22(original): A modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of (i) a gene coding for hTARPP, and/or (ii) a transcription product of the gene coding for hTARPP, and/or (iii) a translation product of the gene coding for hTARPP, and/or (iv) a fragment, or derivative, or variant of (i) to (iii).

Claim 23(original): Use of a modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of (i) a gene coding for hTARPP, and/or (ii) a transcription product of the gene coding for hTARPP,

and/or (iii) a translation product of the gene coding for hTARPP, and/or (iv) a fragment, or derivative, or variant of (i) to (iii) for a preparation of a medicament for treating or preventing a neurodegenerative disease, in particular Alzheimer's disease.

Claim 24(original): A recombinant, non-human animal comprising a non-native gene sequence coding for hTARPP or a fragment, or a derivative, or a variant thereof, said animal being obtainable by:

- (i) providing a gene targeting construct comprising said gene sequence and a selectable marker sequence, and
- (ii) introducing said targeting construct into a stem cell of a non-human animal, and
- (iii) introducing said non-human animal stem cell into a non-human embryo, and
- (iv) transplanting said embryo into a pseudopregnant non-human animal, and
- (v) allowing said embryo to develop to term, and
- (vi) identifying a genetically altered non-human animal whose genome comprises a modification of said gene sequence in both alleles, and
- (vii) breeding the genetically altered non-human animal of step (vi) to obtain a genetically altered non-human animal whose genome comprises a modification of said endogenous gene, wherein said disruption results in said non-human animal exhibiting a predisposition to developing symptoms of a neurodegenerative disease or related diseases or disorders.

Claim 25(original): Use of the recombinant, non-human animal according to claim 24 for screening, testing, and validating compounds, agents, and modulators in the development of

diagnostics and therapeutics to treat neurodegenerative diseases, in particular Alzheimer's disease.

Claim 26(original): An assay for screening for a modulator of neurodegenerative diseases, in particular Alzheimer's disease, or related diseases or disorders of one or more substances selected from the group consisting of

- (i) a gene coding for hTARPP, and/or
- (ii) a transcription product of the gene coding for hTARPP, and/or
- (iii) a translation product of the gene coding for hTARPP, and/or
- (iv) a fragment, or derivative, or variant of (i) to (iii), said method comprising:
 - (a) contacting a cell with a test compound;
 - (b) measuring the activity and/or level of one or more substances recited in (i) to (iv);
 - (c) measuring the activity and/or level of one or more substances recited in (i) to (iv) in a control cell not contacted with said test compound; and
 - (d) comparing the levels and/or activities of the substance in the cells of step (b) and (c), wherein an alteration in the activity and/or level of substances in the contacted cells indicates that the test compound is a modulator of said diseases or disorders.